

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Role, Lorna W.
- (ii) TITLE OF INVENTION: SPLICE VARIANTS OF THE HEREGULIN GENE,
nARIA,
AND USES THEREOF
- (iii) NUMBER OF SEQUENCES: 4
- (iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Cooper & Dunham LLP
(B) STREET: 1185 Avenue of the Americas
(C) CITY: New York
(D) STATE: New York
(E) COUNTRY: U.S.A.
(F) ZIP: 10036
- (v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: White, John P.
(B) REGISTRATION NUMBER: 28,678
(C) REFERENCE/DOCKET NUMBER: 46839-A
- (ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: 212-278-0400
(B) TELEFAX: 212-391-0526

(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3212 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

00312506-051499

Sub
B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

CGGATGCTGC TGCTACTGTC ACTTCTGCCG CTGCCGCTGT TGTTACAGAT TTTGCTTTTG
60
CTCCTTCTAC CGCATGACAA TTGTTTTCTT CGCCTAAGCA GATACCAGCC TCAGATGCTC
120
AAGGTGAGAG TCTTGCCTTT CGCTCTGGGC TATTGGTTCA CTTAATCCGG TCAATTTGTT
180
CGCTGCTCGT GGTGTCTTT CTCCCCGCCC TCCTTCCCCC TGTTTTGTTT TGTTTCGCTT
240
GCTTTCGGGG GGACGCTCCT TCCCTCAGTC AGAAGAGCTG GAATTGCTTG AGAGGCGTAT
300
AAGGAATTAT AAAAGTGGCC AGGAAACACG AGCGCAGTGA CTGCAGAGCT GCCCTTGGCT
360
TCGGCAAGGC AGCGTGAGCG GCAGAGGGCT CGGGCAGGGG GCGGGGGGTC TCCTTTTTCC
420
CGTGCGTTCC TCTTCTCCCA GTTCGGATGA TGTTGCTGTT TCGGACCTCT CGCTGACTCC
480
TGCCCTGTGA TTTTGTCTGA GCGCTGTGAC TGTTACTCCG TCTCTTTCTG TCTGTGTTTC
540
ACAGTAATGG ACTGTGATAG AGTTAAGGCC TTTTGGAGGT GAGCTGTGTC ACAGCTGATG
600
CTTAAACATG TCTGAAGTAG GCACCGAGAC TTTCCCCAGC CCCTCGGCTC AGCTGAGCCC
660
TGATGCATCC CTTGGCGGGC TCCCGGCTGA GGAGAACATG CCGGGGCCCC ACAGAGAGGA
720
CAGCAGGGTC CCAGGTGTGG CAGGCCTGGC CTCGACCTGC TCGTGTGCC TGGAAGCAGA
780
GCGACTGAAG GGCTGCCTCA ACTCTGAGAA GATCTGCATC GCCCCTATCC TGGCTTGCCT
840
GCTCAGCCTC TGCCTCTGCA TTGCTGGCCT CAAGTGGGTC TTTGTGGACA AGATTTTGA
900
GTATGACTCT CCTACACACC TTGACCCTGG GAGGATAGGA CAAGACCCAA GGAGCACTGT
960
GGATCCTACA GCTCTGTCTG CCTGGGTGCC TTCGGAGGTG TATGCCTCAC CCTTCCCCAT

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1020

ACCTAGCCTT GAGAGCAAGG CTGAAGTGAC AGTGCAAAC T GACAGCTCGC TCGTGCCCTC
1080

CAGGCCCTTC CTTCAGCCTT CTCTCTACAA CCGCATCCTA GATGTCGGGT TGTGGTCCTC
1140

TGCCACACCG TCACTGTCAC CATCCTCCCT GGAGCCTACC ACGGCATCTC AGGCACAAGC
1200

AACAGAAACC AATCTCCAAA CTGCTCCAAA ACTTTCCACT TCTACATCTA CAACTGGGAC
1260

AAGTCATCTC ACAAAATGTG ACATAAAGCA GAAAGCCTTC TGTGTAAATG GGGGAGAGTG
1320

CTACATGGTT AAAGACCTCC CAAACCCTCC ACGATACCTA TGCAGGTGCC CAAATGAATT
1380

TACTGGTGAT CGCTGCCAAA ACTACGTAAT GGCCAGCTTC TACAAGCATC TTGGGATTGA
1440

ATTTATGGAA GCTGAGGAAC TGTACCAGAA ACGGGTGCTG ACCATAACTG GCATTTGCAT
1500

TGCTCTTCTA GTAGTTGGCA TCATGTGTGT GGTGGCCTAC TGCAAAACCA AGAAGCAGAG
1560

GAAAAAGTTG CATGACCGCC TTCGGCAGAG CCTTCGCTCA GAGAGGAACA ACGTTATGAA
1620

CATGGCAAAT GGGCCACACC ACCCCAACCC ACCACCAGAC AATGTCCAGC TGGTGAATCA
1680

GTACGTTTCA AAAAACATAA TCTCCAGTGA ACGTGTCGTT GAGCGAGAAA CCGAGACCTC
1740

GTTTTCCACA AGCCACTACA CCTCAACAAC TCATCACTCC ATGACAGTCA CCCAGACGCC
1800

TAGCCACAGC TGGAGTAATG GCCATACCGA AAGCATTCTC TCCGAAAGCC ACTCCGTGCT
1860

CGTCAGCTCC TCAGTGGAGA ATAGCAGGCA CACCAGCCCA ACAGGGCCAC GAGGCCGCCT
1920

CAATGGCATT GGTGGGCCAA GGGAAGGCAA CAGCTTCCTC CGGCATGCAA GAGAGACCCC
1980

TGACTCCTAC CGAGACTCTC CTCACAGTGA AAGGTATGTC TCAGCTATGA CCACACCAGC
2040

0012506-05149

TCGCATGTCA CCCGTTGATT TCCACACTCC AACTTCTCCC AAGTCCCCTC CATCTGAAAT
2100

GTCACCACCA GTTTCAGCT TGACCATCTC CATCCCTTCG GTGGCGGTGA GTCCCTTTAT
2160

GGACGAGGAG AGACCGCTGC TGTGTTGAC CCCACCACGG CTGCGTGAGA AGTACGACAA
2220

CCACCTTCAG CAATTCAACT CCTTCCACAA CAATCCCACC CATGAGAGCA ACAGTCTGCC
2280

ACCCAGTCCT CTGAGGATAG TGGAGGATGA AGAGTATGAG ACCACGCAGG AGTACGAACC
2340

AGCACAGGAG CCTCCAAAGA AACTCACCAA CAGCCGGAGG GTGAAAAGAA CAAAGCCCAA
2400

TGGCCATATT TCCAGCAGGG TAGAAGTGGA CTCCGACACA AGCTCTCAGA GCACTAGCTC
2460

TGAGAGCGAA ACAGAAGATG AAAGAATAGG TGAGGATACA CCATTTCTTA GCATACAAAA
2520

TCCCATGGCA ACCAGTCTGG AGCCAGCCGC TGCATATCGG CTGGCTGAGA ACAGGACTAA
2580

CCCGGCAAAT CGCTTCTCCA CACCAGAAGA GTTGCAAGCA AGGTTGTCCA GTGTAATAGC
2640

TAACCAAGAC CCTATTGCTG TATAAGACAT AAACAAAACA CATAGATTCA CATGTAAAAC
2700

TTTATTTTAT ATAATGAAGT ATTCCACCTT TAAATTAAAC AATTTATTTT ATTTTAGCAA
2760

TTCCGCTGAT AGAAAACAAG AGTGGAAAAA GAAACTTTTA TAAATTAAGT ATACGTATGT
2820

ACAAATGTGT TATGTGCCAT ATGTAGCAAT TTTTACAGT ATTTCCAAAA TGGGGAAAGA
2880

TATCAATGGT GCCTTTATGT TATGTTATGT TGAGAGCAAG TTTTGTACAG CTACAATGAT
2940

TGCTGTCCCG TAGTATTTTG CAAAACCTTC TAGCCCTCAG TTGTTCTGGC TTTTTTGTGC
3000

ATTGCATTAT AATGACTGGA TGTATGATTT GCAAGAATTG CAGAAGTCCC CATTTGCTTG
3060

TTGTGGAATC CCCAGATCAA AAAGCCCTGT TATGGCACTC ACACCCTATC CACTTCACCA

3120

GGAAAAAAAA AAAATCAAAA AAAAAAAAAA AAAAAAAGA AAAGAAAGAG AAAAAAGAAA
3180

AGAAAAAGAA AAAAAAAGCT GAAAAAATAA AA
3212

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1070 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Arg Gly Cys Cys Cys Tyr Cys His Phe Cys Arg Cys Arg Cys Cys Tyr
1 5 10 15

Xaa Phe Cys Phe Cys Ser Phe Tyr Arg Met Thr Ile Val Phe Leu Ala
20 25 30

Leu Ala Asp Thr Ser Leu Arg Cys Ser Arg Xaa Glu Ser Cys Leu Ser
35 40 45

Gly Trp Ala Ile Gly Ser Leu Asn Pro Val Asn Leu Phe Ala Ala Arg
50 55 60

Leu Cys Leu Ser Pro Arg Pro Pro Ser Pro Cys Phe Val Leu Phe Arg
65 70 75 80

Leu Leu Ser Gly Gly Arg Ser Phe Pro Gln Ser Glu Glu Leu Glu Leu
85 90 95

Gln	Glu Arg Arg Ile Arg Asn Tyr Lys Ser Gly Gln Glu Thr Arg Ala	
	100	105 110
Arg	Xaa Leu Gln Ser Cys Pro Trp Leu Arg Gln Gly Ser Val Ser Gly	
	115	120 125
Ser	Gly Leu Gly Gln Gly Ala Gly Gly Leu Leu Phe Pro Val Arg Ser	
	130	135 140
Pro	Ser Pro Ser Ser Asp Asp Val Ala Val Ser Asp Leu Ser Leu Thr	
160	145	150 155
Ser	Ala Leu Xaa Phe Leu Leu Ser Ala Val Thr Val Thr Pro Ser Leu	
	165	170 175
Gly	Val Cys Val Ser Gln Xaa Trp Thr Val Ile Glu Leu Arg Pro Phe	
	180	185 190
Thr	Gly Glu Leu Cys His Ser Xaa Cys Leu Asn Met Ser Glu Val Gly	
	195	200 205
Leu	Glu Thr Phe Pro Ser Pro Ser Ala Gln Leu Ser Pro Asp Ala Ser	
	210	215 220
Asp	Gly Gly Leu Pro Ala Glu Glu Asn Met Pro Gly Pro His Arg Glu	
240	225	230 235
Cys	Ser Arg Val Pro Gly Val Ala Gly Leu Ala Ser Thr Cys Cys Val	
	245	250 255
Cys	Leu Glu Ala Glu Arg Leu Lys Gly Cys Leu Asn Ser Glu Lys Ile	

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	260	265	270
Ala	Ile Ala Pro Ile Leu Ala Cys Leu Leu Ser Leu Cys Leu Cys Ile		
	275	280	285
Pro	Gly Leu Lys Trp Val Phe Val Asp Lys Ile Phe Glu Tyr Asp Ser		
	290	295	300
Val	Thr His Leu Asp Pro Gly Arg Ile Gly Gln Asp Pro Arg Ser Thr		
320	305	310	315
Ser	Asp Pro Thr Ala Leu Ser Ala Trp Val Pro Ser Glu Val Tyr Ala		
	325	330	335
Gln	Pro Phe Pro Ile Pro Ser Leu Glu Ser Lys Ala Glu Val Thr Val		
	340	345	350
Leu	Thr Asp Ser Ser Leu Val Pro Ser Arg Pro Phe Leu Gln Pro Ser		
	355	360	365
Ser	Tyr Asn Arg Ile Leu Asp Val Gly Leu Trp Ser Ser Ala Thr Pro		
	370	375	380
Ala	Leu Ser Pro Ser Ser Leu Glu Pro Thr Thr Ala Ser Gln Ala Gln		
400	385	390	395
Ser	Thr Glu Thr Asn Leu Gln Thr Ala Pro Lys Leu Ser Thr Ser Thr		
	405	410	415
Ala	Thr Thr Gly Thr Ser His Leu Thr Lys Cys Asp Ile Lys Gln Lys		
	420	425	430

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Asn	Phe	Cys	Val	Asn	Gly	Gly	Glu	Cys	Tyr	Met	Val	Lys	Asp	Leu	Pro
			435					440					445		
Arg	Pro	Pro	Arg	Tyr	Leu	Cys	Arg	Cys	Pro	Asn	Glu	Phe	Thr	Gly	Asp
			450				455					460			
Glu	Cys	Gln	Asn	Tyr	Val	Met	Ala	Ser	Phe	Tyr	Lys	His	Leu	Gly	Ile
480	465					470					475				
Thr	Phe	Met	Glu	Ala	Glu	Glu	Leu	Tyr	Gln	Lys	Arg	Val	Leu	Thr	Ile
					485					490				495	
Ala	Gly	Ile	Cys	Ile	Ala	Leu	Leu	Val	Val	Gly	Ile	Met	Cys	Val	Val
				500					505				510		
Arg	Tyr	Cys	Lys	Thr	Lys	Lys	Gln	Arg	Lys	Lys	Leu	His	Asp	Arg	Leu
			515					520					525		
Gly	Gln	Ser	Leu	Arg	Ser	Glu	Arg	Asn	Asn	Val	Met	Asn	Met	Ala	Asn
		530					535					540			
Gln	Pro	His	His	Pro	Asn	Pro	Pro	Pro	Asp	Asn	Val	Gln	Leu	Val	Asn
560	545					550					555				
Glu	Tyr	Val	Ser	Lys	Asn	Ile	Ile	Ser	Ser	Glu	Arg	Val	Val	Glu	Arg
					565					570				575	
His	Thr	Glu	Thr	Ser	Phe	Ser	Thr	Ser	His	Tyr	Thr	Ser	Thr	Thr	His
				580					585				590		
His	Ser	Met	Thr	Val	Thr	Gln	Thr	Pro	Ser	His	Ser	Trp	Ser	Asn	Gly

	595	600	605
Ser	Thr Glu Ser Ile Leu Ser Glu Ser His Ser Val Leu Val Ser Ser		
	610	615	620
Leu	Val Glu Asn Ser Arg His Thr Ser Pro Thr Gly Pro Arg Gly Arg		
640	625	630	635
Ala	Asn Gly Ile Gly Gly Pro Arg Glu Gly Asn Ser Phe Leu Arg His		
	645	650	655
Tyr	Arg Glu Thr Pro Asp Ser Tyr Arg Asp Ser Pro His Ser Glu Arg		
	660	665	670
His	Val Ser Ala Met Thr Thr Pro Ala Arg Met Ser Pro Val Asp Phe		
	675	680	685
Val	Thr Pro Thr Ser Pro Lys Ser Pro Pro Ser Glu Met Ser Pro Pro		
	690	695	700
Met	Ser Ser Leu Thr Ile Ser Ile Pro Ser Val Ala Val Ser Pro Phe		
720	705	710	715
Glu	Asp Glu Glu Arg Pro Leu Leu Leu Val Thr Pro Pro Arg Leu Arg		
	725	730	735
Pro	Lys Tyr Asp Asn His Leu Gln Gln Phe Asn Ser Phe His Asn Asn		
	740	745	750
Glu	Thr His Glu Ser Asn Ser Leu Pro Pro Ser Pro Leu Arg Ile Val		
	755	760	765

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Pro	Asp	Glu	Glu	Tyr	Glu	Thr	Thr	Gln	Glu	Tyr	Glu	Pro	Ala	Gln	Glu
	770							775						780	
Asn	Pro	Lys	Lys	Leu	Thr	Asn	Ser	Arg	Arg	Val	Lys	Arg	Thr	Lys	Pro
800	785					790					795				
Gln	Gly	His	Ile	Ser	Ser	Arg	Val	Glu	Val	Asp	Ser	Asp	Thr	Ser	Ser
						805				810				815	
Asp	Ser	Thr	Ser	Ser	Glu	Ser	Glu	Thr	Glu	Asp	Glu	Arg	Ile	Gly	Glu
					820					825				830	
Pro	Thr	Pro	Phe	Leu	Ser	Ile	Gln	Asn	Pro	Met	Ala	Thr	Ser	Leu	Glu
			835					840						845	
Arg	Ala	Ala	Ala	Tyr	Arg	Leu	Ala	Glu	Asn	Arg	Thr	Asn	Pro	Ala	Asn
		850						855						860	
Ala	Phe	Ser	Thr	Pro	Glu	Glu	Leu	Gln	Ala	Arg	Leu	Ser	Ser	Val	Ile
880	865						870					875			
Phe	Asn	Gln	Asp	Pro	Ile	Ala	Val	Xaa	Asp	Ile	Asn	Lys	Thr	His	Arg
						885					890				895
Leu	Thr	Cys	Lys	Thr	Leu	Phe	Tyr	Ile	Met	Lys	Tyr	Ser	Thr	Phe	Lys
					900					905					910
Trp	Asn	Asn	Leu	Phe	Tyr	Phe	Ser	Asn	Ser	Ala	Asp	Arg	Lys	Gln	Glu
			915					920					925		
Tyr	Lys	Lys	Lys	Leu	Leu	Xaa	Ile	Lys	Tyr	Thr	Tyr	Val	Gln	Met	Cys

	930	935	940
Asp	Val Pro Tyr Val Ala Ile Phe Tyr Ser Ile Ser Lys Met Gly Lys		
960	945	950	955
Thr	Ile Asn Gly Ala Phe Met Leu Cys Tyr Val Glu Ser Lys Phe Cys		
	965	970	975
Pro	Ala Thr Met Ile Ala Val Pro Xaa Tyr Phe Ala Lys Pro Ser Ser		
	980	985	990
Tyr	Gln Leu Phe Trp Leu Phe Cys Ala Leu His Tyr Asn Asp Trp Met		
	995	1000	1005
Pro	Asp Leu Gln Glu Leu Gln Lys Ser Pro Phe Ala Cys Cys Gly Ile		
	1010	1015	1020
Gln	Arg Ser Lys Ser Pro Val Met Ala Leu Thr Pro Tyr Pro Leu His		
1040	1025	1030	1035
Arg	Glu Lys Lys Lys Ile Lys Lys Lys Lys Lys Lys Lys Lys Arg Lys Glu		
	1045	1050	1055
	Glu Lys Arg Lys Glu Lys Glu Lys Lys Ser Xaa Lys Asn Lys		
	1060	1065	1070

(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1351 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

CGGCCTGTAA GATGCTGTAT CATTTGGTTG GGGGGGCCTC TGCGTGGTAA TGGACCGTGA
60

GAGCGGCCAG GCCTTCTTCT GGAGGTGAGC CGATGGAGAT TTATTCCCCA GACATGTCTG
120

AGGTCGCCGC CGAGAGGTCC TCCAGCCCCT CCACTCAGCT GAGTGCAGAC CCATCTCTTG
180

ATGGGCTTCC GGCAGCAGAA GACATGCCAG AGCCCCAGAC TGAAGATGGG AGAACCCCTG
240

GACTCGTGGG CCTGGCCGTG CCCTGCTGTG CGTGCCTAGA AGCTGAGCGC CTGAGAGGTT
300

GCCTCAACTC AGAGAAAATC TGCATTGTCC CCATCCTGGC TTGCCTGGTC AGCCTCTGCC
360

TCTGCATCGC CGGCCTCAAG TGGGTATTTG TGGACAAGAT CTTTGAATAT GACTCTCCTA
420

CTCACCTTGA CCCTGGGGGG TTAGGCCAGG ACCCTATTAT TTCTCTGGAC GCAACTGCTG
480

CCTCAGCTGT GTGGGTGTCT TCTGAGGCAT AACTTCACC TGTCTCTAGG GCTCAATCTG
540

AAAGTGAGGT TCAAGTTACA GTGCAAGGTG ACAAGGCTGT TGTCTCCTTT GAACCATCAG
600

CGGCACCGAC ACCGAAGAAT CGTATTTTTG CCTTTTCTTT CTTGCCGTCC ACTGCGCCAT
660

CCTTCCCTTC ACCCACCCGG AACCCTGAGG TGAGAACGCC CAAGTCAGCA ACTCAGCCAC
720

AAACAACAGA AACTAATCTC CAACTGCTC CTAAACTTTC TACATCTACA TCCACCACTG
780

GGACAAGCCA TCTTGTAATA TGTGCGGAGA AGGAGAAAAC TTTCTGTGTG AATGGAGGGG
840

AGTGCTTCAT GGTGAAAGAC CTTTCAAACC CCTCGAGATA CTTGTGCAAA GGCGGAGGAG
900

CTGTACCAGA AGAGAGTGCT GACCATAACC GGCATCTGCA TCGCCCTCCT TGTGGTCGGC
960

ATCATGTGTG TGGTGGCCTA CTGCAAAACC AAGAAACAGC GGAAAAAGCT GCATGACCGT
1020

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CTTCGGCAGA GCCTTCGGTC TGAACGAAAC AATACGATGA ACATTGCCAA TGGGCCTCAC
1080

CATCCTAACC CACCCCCCGA GAATGTCCAG CTGGTGAATC AATACGTATC TAAAAACGTC
1140

ATCTCCAGTG AGCATATTGT TGAGAGAGAA GCAGAGACAT CCTTTTCCAC CAGTCACTAT
1200

ACTTCCACAG CCCATCACTC CACTACTGTC ACCCAGACTC CTAGCCACAG CTGGAGCAAC
1260

GGACACACTG AAAGCATCCT TTCCGAAAGC CACTCTGTAA TCGTGATGTC ATCCGTAGAA
1320

AACAGTAGGC ACAGCAGCCC AACTGGGGCC G
1351

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 449 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Xaa	Ala	Cys	Lys	Met	Leu	Tyr	His	Leu	Val	Gly	Gly	Ala	Ser	Ala	Trp
	1				5					10					15
Glu	Trp	Thr	Val	Arg	Ala	Ala	Arg	Pro	Ser	Ser	Gly	Gly	Glu	Pro	Met
					20					25				30	
Ser	Ile	Tyr	Ser	Pro	Asp	Met	Ser	Glu	Val	Ala	Ala	Glu	Arg	Ser	Ser
					35					40				45	
Ala	Pro	Ser	Thr	Gln	Leu	Ser	Ala	Asp	Pro	Ser	Leu	Asp	Gly	Leu	Pro
					50					55				60	

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Gly	Ala	Glu	Asp	Met	Pro	Glu	Pro	Gln	Thr	Glu	Asp	Gly	Arg	Thr	Pro
	65					70				75					80
Arg	Leu	Val	Gly	Leu	Ala	Val	Pro	Cys	Cys	Ala	Cys	Leu	Glu	Ala	Glu
						85				90					95
Leu	Leu	Arg	Gly	Cys	Leu	Asn	Ser	Glu	Lys	Ile	Cys	Ile	Val	Pro	Ile
					100				105					110	
Val	Ala	Cys	Leu	Val	Ser	Leu	Cys	Leu	Cys	Ile	Ala	Gly	Leu	Lys	Trp
			115					120					125		
Pro	Phe	Val	Asp	Lys	Ile	Phe	Glu	Tyr	Asp	Ser	Pro	Thr	His	Leu	Asp
			130					135					140		
Ala	Gly	Gly	Leu	Gly	Gln	Asp	Pro	Ile	Ile	Ser	Leu	Asp	Ala	Thr	Ala
	145					150						155			
Arg	Ser	Ala	Val	Trp	Val	Ser	Ser	Glu	Ala	Tyr	Thr	Ser	Pro	Val	Ser
					165					170					175
Ala	Ala	Gln	Ser	Glu	Ser	Glu	Val	Gln	Val	Thr	Val	Gln	Gly	Asp	Lys
					180				185					190	
Ile	Val	Val	Ser	Phe	Glu	Pro	Ser	Ala	Ala	Pro	Thr	Pro	Lys	Asn	Arg
			195					200					205		
Pro	Phe	Ala	Phe	Ser	Phe	Leu	Pro	Ser	Thr	Ala	Pro	Ser	Phe	Pro	Ser
		210					215					220			
Gln	Thr	Arg	Asn	Pro	Glu	Val	Arg	Thr	Pro	Lys	Ser	Ala	Thr	Gln	Pro

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240	225		230			235									
Thr	Thr	Thr	Glu	Thr	Asn	Leu	Gln	Thr	Ala	Pro	Lys	Leu	Ser	Thr	Ser
					245					250				255	
Lys	Ser	Thr	Thr	Gly	Thr	Ser	His	Leu	Val	Lys	Cys	Ala	Glu	Lys	Glu
				260					265					270	
Ser	Thr	Phe	Cys	Val	Asn	Gly	Gly	Glu	Cys	Phe	Met	Val	Lys	Asp	Leu
			275					280					285		
Glu	Asn	Pro	Ser	Arg	Tyr	Leu	Cys	Lys	Gly	Gly	Gly	Ala	Val	Pro	Glu
		290						295					300		
His	Ser	Ala	Asp	His	Asn	Arg	His	Leu	His	Arg	Pro	Pro	Cys	Gly	Arg
320			305					310					315		
Ala	His	Val	Cys	Gly	Gly	Leu	Leu	Gln	Asn	Gln	Glu	Thr	Ala	Glu	Lys
						325				330				335	
Asp	Ala	Xaa	Pro	Ser	Ser	Ala	Glu	Pro	Ser	Val	Xaa	Thr	Lys	Gln	Tyr
					340				345					350	
Cys	Glu	His	Cys	Gln	Trp	Ala	Ser	Pro	Ser	Xaa	Pro	Thr	Pro	Arg	Glu
			355					360					365		
Ala	Pro	Ala	Gly	Glu	Ser	Ile	Arg	Ile	Xaa	Lys	Arg	His	Leu	Gln	Xaa
		370						375					380		
Tyr	Tyr	Cys	Xaa	Glu	Arg	Ser	Arg	Asp	Ile	Leu	Phe	His	Gln	Ser	Leu
400		385						390					395		

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Gln

Cys

Trp

Gly

Sub
D1
CNT

Year	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	